REMARKS

Claims 18, 21-25, 28 and 39-58 were pending in the instant application. Claim 18 has been amended. Accordingly, upon entry of the present Amendment, claims 18, 21-25, 28 and 39-58 will remain pending in the application.

Applicants respectfully submit that no new matter has been introduced by the foregoing claim amendments. Support for the claim amendments and the new claims presented herein may be found throughout the originally filed application and claims. Specifically, support for the amendments to claim 18 can be found at least in Figure 1A, as filed, and at least at paragraphs [023]-[025] of the specification as filed.

Amendment and/or cancellation of the claims is not to be construed as acquiescence to any of the objections/rejections set forth in the instant Office Action and was done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims, as originally filed, or similar claims in this or one or more subsequent patent applications.

Acknowledgement of Withdrawal of Previous Rejections

Applicants gratefully acknowledge the withdrawal of the previous objection to the specification for containing embedded hyperlink and/or other form of browser-executable code.

Rejection of Claims 18, 21-25 and 28 Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 18, 21-25 and 28 under 35 U.S.C. § 103(a) as being unpatentable over Fischer (U.S. Patent No. 6,939,543) in view of Patti (U.S. Patent No. 6,703,025). Specifically, the Examiner is of the opinion that

> Fischer et al in view of Patti et al provide guidance, teaching, suggestion and motivation to make monoclonal, chimeric, humanized and human antibodies to ribitol teichoic acid, a wall component of known human pathogenic strains of Staphylococcus aureus because Fischer et al teach antibodies directed to lipoteichoic acids "can block the binding of Gram positive bacteria to epithelial cells, such as human epithelial cells (Fischer et al, first paragraph)" and Patti et al teach ribitol phosphate is immunogenic and induces antibodies directed to S. aureus LTA.

> It is obvious to make a monoclonal antibody to an antigen for which polyclonal antibodies have been made. In re Erlich, 1988. Fischer et al in view of Patti et al. obviate the instant invention as now claimed.

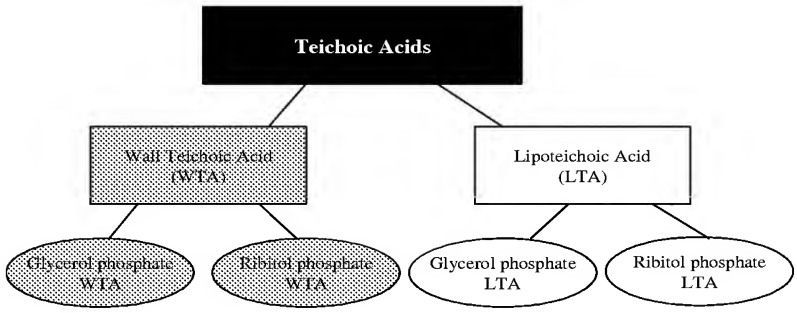
Applicants respectfully traverse this rejection on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness since neither Fischer nor Patti, alone or in combination, teach or suggest the claimed invention and further fail to provide the necessary motivation or reasonable expectation of success for the ordinarily skilled artisan to arrive at the presently claimed invention.

To establish a *prima facie* case of obviousness, it is necessary for the Examiner to apply a flexible teaching, suggestion, or motivation test to combine known elements in order to show that the combination is obvious. *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). Importantly, the *KSR* Court noted that "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." (*In re Kahn*, 441 F.3d 911,988 (CA Fed. 2006) cited with approval in KSR).

The test for *prima facie* obviousness is consistent with the legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.,* 127 S. Ct. 1727 (2007). *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.,* 492 F.3d 1350, 1356 (Fed. Cir. 2007). "While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test, the Court acknowledged the importance of identifying 'a *reason* that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Id.* (quoting *KSR,* 127 S. Ct. at 1731) (emphasis added). Although the TSM test should not be applied in a rigid manner, it can provide helpful insight to an obviousness inquiry. *KSR,* 127 S. Ct. at 1731. The *KSR* Court upheld the secondary considerations of non-obviousness, noting that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* Although the prior art reference, or references when combined, need not teach or suggest all of the claim limitations, a *reason* must be given why the differences between the prior art and the claimed limitation would have been obvious to one of skill in the art (see Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103, Federal Register, Vol. 72, No. 195).

The claims, as amended are directed to a pharmaceutical composition comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that ***specifically binds to a ribitol phosphate wall teichoic acid (WTA) of Figure 1A of S. aureus***, wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks ***nasal colonization*** or infection by *S. aureus* upon administration to a patient.

To begin with, Applicants provide herein scientific background information relating to the differences between LTA and WTA. Most Gram-positive bacteria have two types of teichoic acids, one covalently linked to the peptidoglycan, which is referred to as wall teichoic acid (WTA), and one anchored to the cell membrane via a lipid with its chain extending into the bacterial cell wall, which is referred to as lipoteichoic acid (LTA) (for a review see, *e.g.*, Weidenmaier and Peschel, 2008, attached herein as Appendix A). The types of teichoic acids are depicted below.

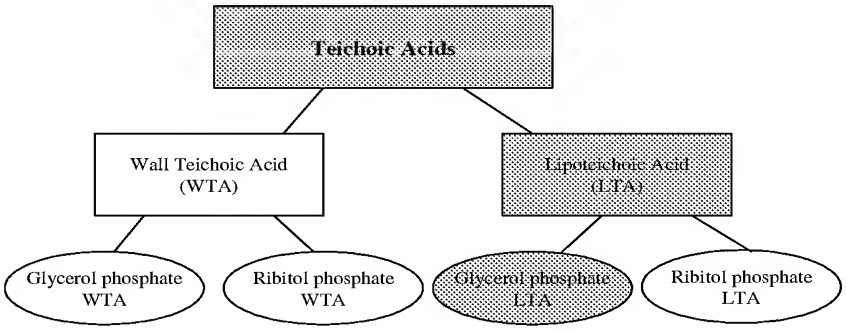


Teichoic acids differ according to their type of sugar, net charge, and decoration of repeating units. Staphylococci can contain either glycerol phosphate or ribitol phosphate as the repeating unit in the WTA (see, *e.g.*, Figure 2B on page 688 of Neuhaus and Baddiley, 2003, attached herein as Appendix B). Staphylococci can also contain either glycerol phosphate or ribitol phosphate as the repeating unit in the LTA. WTA and LTA are assembled via different pathways in the cell (see *e.g.*, page 689 of Neuhaus and Baddiley). Additionally, the stereochemistry of LTAs and the biosynthetic origin of the glycerol phosphates are different from those of WTA (see, *e.g.*, page 3, left column, third paragraph of Weidenmaier and Peschel).

The instant invention is specifically directed to antibodies which bind the ribitol WTA (as shown in Figure 1A) of *S. aureus*. Applicants wish to point out to the Examiner that the LTA of this species of Staphylococci, *S. aureus*, is composed of glycerol phosphate, while the WTA of *S. aureus* is composed of ribitol phosphate. Please see Figure 2 of Weidenmaier and

Peschel, which schematically depicts the structural differences between the WTA and LTA of *S. aureus*. The presently claimed invention is directed to antibodies which specifically bind ribitol phosphate WTA of *S. aureus,* which is a very different molecule than the glycerol phosphate LTA of *S. epidermidis* in the Fischer patent, as described in more detail below.

The Examiner states that "Fischer... suggests antibodies to glycerol and ribitol phosphate antigens." Applicants respectfully submit that this statement mischaracterizes the teachings of Fischer. Specifically, Fischer (at column 5, lines 34-36) merely *defines* teichoic acids according to the scientific dictionary definition, as described above, that teichoic acids (such as WTA and LTA) can be either polymers of glycerol or ribitol phosphate. With respect to antibodies to teichoic aid, however, Fischer specifically states that *"[t]he teichoic acids related to this invention are* ***lipoteichoic acids[LTA] which are acids made up of glycerol phosphate***" (see column 5, lines 40-43) (emphasis added), as depicted below.



Indeed, the only mention of the term "ribitol" in the entire Fischer patent is located in column 5, lines 31-36, in the scientific background section of the patent, where they set forth the dictionary description of the term "teichoic acid", as discussed above. Therefore, the Examiner's assertion that "Fischer et al describe combination compositions of antibodies for antibody therapy...and obtain the combination composition of antibodies by immunization of mixtures of antigens to include both types of teichoic acid antigens" is unfounded, as Fischer does not teach or suggest antibodies to wall teichoic acids (WTA), to ribitol wall teichoic acids, or to the specific ribitol teichoic acid of *S. aureus* as set forth in Figure 1A of the instant application.

Moreover, in contrast to the instant invention, Fischer immunized mice with whole *S. epidermidis*, Strain Hay (see, *e.g.,* column 16, lines 10-14 of Fischer), removed the mice spleens, prepared hybridoma cell suspensions and tested hybridoma supernatants for the presence of antibodies reactive with methanol-fixed *S. epidermidis* (see, *e.g.,* columns 16-17, specifically column 17, lines 5-13 of Fischer). Applicants respectfully submit that the glycerol phosphate

teichoic acids of *S. epidermidis* are completely distinct from the ribitol phosphate teichoic acids of Figure 1A of *S. aureus*, as claimed. Specifically, it is well known in the art that the wall teichoic acid of *S. epidermidis* ***only contains glycerol phosphate teichoic acids and does not contain ribitol phosphate teichoic acids***. For example, please see Table 3 of Endl *et al.* (*Arch. Microbiol.,* 137:272-280, 1984), attached herein as Appendix C, and Table 1 of Endl *et al.* (*Arch. Microbiol.* 135:215-223, 1983), attached herein as Appendix D, which demonstrate that the sole teichoic acid component of several different strains of *S. epidermidis* is glycerol phosphate and not ribitol phosphate. In contrast, the claimed antibodies of the instant invention specifically bind to the ribitol phosphate WTA of Figure 1A of *S. aureus*. Therefore, the Examiner's assertion that "Fischer teaches and suggests combination compositions of antibodies directed to ribitol phosphate and glycerol phosphate antigens" is unfounded, as Fischer does not teach or suggest either antibodies to wall teichoic acids (WTA), antibodies to ribitol wall teichoic acids, or antibodies to the specific ribitol teichoic acid of *S. aureus* as set forth in Figure 1A of the instant application.

Applicants point out that the courts have emphasized that "[a] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of argument reliant upon ex post reasoning." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. at 1742. Accordingly, "[a] flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis." *In re Translogic Tech.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

Applicants further point out that the pending claims require that the antibody ***specifically bind*** to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. As such, the claimed antibodies are ***specific*** for the ribitol phosphate WTA of *S. aureus* (as shown in Figure 1A) and ***would not significantly cross-react*** with glycerol phosphate LTA, ribitol phosphate LTA or peptidoglycan. Moreover, the Fischer reference fails to provide any teaching or suggestion that therapeutically effective amounts of antibodies to the ribitol wall teichoic acid of Figure 1A of *S. aureus* could be used to alleviate or block ***nasal colonization or infection*** by *S. aureus*. Thus, it would not be obvious to one of ordinary skill in the art to make antibodies which specifically bind to the ribitol phosphate WTA of Figure 1A of *S. aureus* based on the teachings of Fischer.

Te secondary reference of Patti fails to make up for the aforementioned deficiencies in the primary reference of Fischer. Specifically, Patti is directed to the use of MSCRAMMs

(Microbial Surface Components Recognizing Adhesive Matrix Molecules) or antibodies thereof in multicomponent vaccines. The reference discloses that ligand binding domains in MSCRAMMs are defined by relatively short contiguous stretches of amino acid sequences (motifs) (see Column 2, lines 55-58) and is directed to ***protein*** components of organisms rather than non-protein components (such as teichoic acids) (see Column 6, lines 31-35). In fact, the term "teichoic acid" is only used in two paragraphs of the entire Patti reference. Specifically, the Patti reference states that

> [a]s used herein, an "antigenically functional equivalent" protein or peptide is one that incorporates an epitope that is one that is ***immunologically cross-reactive*** with one or more epitopes either derived from any of the MSCRAMM proteins disclosed... or derived from any of the particular bacterial components disclosed (e.g., teichoic acids, alpha toxin and capsular polysaccharide type 5). (Emphasis added).

and that

> [t]eichoic acids, ***lipoteichoic acid*** for example, which are polymers of glycerol or ribitol phosphate, are linked to the peptidoglycan and can be antigenic. Antiteichoic antibodies are detectable by gel diffusion may be found in patients with active endocarditis due to *S. aureus*. (Emphasis added).

(see column 12, lines 57-67 and column 22, lines 48-52). In these paragraphs, Patti *et al.* simply note that antiteichoic antibodies may be detected in some patients, however, it is unclear whether antibodies to teichoic acids are detectable. In fact, nowhere does Patti *et al.* teach or suggest that ***anti-WTA antibodies, specifically, antibodies specific for WTA which are polymers of ribitol phosphate,*** are detectable in patients with active endocarditis. Thus, the conclusion reached by the examiner that "Patti et al [shows] that ribitol phosphate is immunogenic, and induces antibodies, wherein polyclonal antibodies to ribitol phosphate have been made" cannot be inferred from the reference.

Furthermore, and as set forth in the previous reply, the only reference to monoclonal antibodies in Patti relates ***specifically to antibodies specific for MSCRAMM peptides***, not to antibodies that bind to any type of teichoic acid, let alone to WTA, ribitol WTA, or the ribitol WTA as specifically shown in Figure 1A of *S. aureus*. The reference further fails to provide any suggestion that antibodies to the ribitol wall teichoic acid of Figure 1A of *S. aureus* could be administered to ***alleviate or block nasal colonization or infection*** by *S. aureus*.

The Examiner states that the Patti reference "goes beyond just discussing proteins and describes utilizing teichoic acid epitopes to stimulate antibodies that induce ***cross reactive antibodies***, as well as teaches glycerol and ribitol phosphate induce anti-teichoic antibodies" (emphasis added). However, as described above, the pending claims require that the antibody ***specifically bind*** to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. As such, the claimed antibodies are ***specific*** for the ribitol phosphate WTA of *S. aureus* (as shown in Figure 1A) and ***would <u>not</u> be cross reactive***, as alleged by the Examiner. Thus, it would not be obvious to one of ordinary skill in the art to make antibodies which ***specifically*** bind to the ribitol phosphate WTA of Figure 1A of *S. aureus* based on the teachings of Patti, alone or in combination with the teachings of Fischer, as neither Fischer nor Patti teach or suggest antibodies which ***specifically bind*** the ribitol teichoic acid of *S. aureus* as set forth in Figure 1A of the instant claims. Accordingly, the claimed antibodies would not be obvious to one of ordinary skill in the art.

Furthermore, as set forth above, neither Fischer *et al.* nor Patti *et al.*, either alone or in combination, teach or suggest a pharmaceutical compositions comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that ***specifically*** binds to a ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus,* wherein said therapeutically effective amount of said antibody or fragment thereof ***alleviates or blocks nasal colonization or infection by S. aureus*** upon administration to a patient. Accordingly, Applicants respectfully request that the rejection of claims 18, 21-25 and 28 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Rejection of Claims 18 and 25 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 18 and 25 under 35 U.S.C. §112, first paragraph because allegedly the specification,

> ***while being enabling for*** a method of producing a humanized antibody or a humanized single-chain Fv (scFv), or fragments thereof comprising both VH and VL domains, wherein the humanized antibody, the humanized scFv, and fragments thereof comprise 6 CDRs, three from the VH domain and three from the VL domain, wherein the humanized antibody, the humanized scFV and fragments thereof ***bind the same antigen*** as the parental non-human antibody, does not reasonably provide enablement for a

> humanized variable domain, a humanized antibody, a humanized scFv and fragments thereof that ***do not bind to the same antigen*** and the whole antibody ***or bind a different antigen*** than the parental non-human antibody as broadly encompassed by the claims. (Emphasis added).

Applicants traverse the foregoing rejection on the grounds that the amount of direction and guidance disclosed in the specification is sufficient to enable the skilled artisan to make and use the claimed invention using only routine experimentation.

Without acquiescing to the Examiner's rejection, the claims have been amended to be directed to a pharmaceutical composition comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that ***specifically binds to a ribitol phosphate wall teichoic acid (WTA) of Figure 1A of S. aureus***, wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks nasal colonization or infection by *S. aureus* upon administration to a patient. For the reasons provided below and the reasons already of record, Applicants respectfully submit that the instant specification enables the ordinary skilled artisan to make and use the claimed compounds using only routine experimentation.

To begin with, the Examiner alleges that claim 25 includes "humanized scFv and fragments which need not bind antigen or bind a different antigen that the parental non-human antibody". In contrast to the Examiner's assertion, the pending claims require that the antibody or antigen-binding fragment thereof ***specifically binds*** to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. As discussed above, Applicants state for the record that the claimed antibodies are ***specific*** for the ribitol phosphate WTA of *S. aureus* (as shown in Figure 1) and ***would <u>not</u> bind a different antigen or be non-antigen binding***, as alleged by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

The Examiner has also alleged that the specification "does not enable humanized variable domains, humanized antibodies, humanized scFvs and fragments thereof, which do not contain the necessary CDRs." The Examiner recognizes that the specification is "enabling for a method of producing a humanized antibody or a humanized single-chain Fv (scFv), or fragments thereof comprising both VH and VL domains, wherein the humanized antibody, the humanized scFv, and fragments thereof comprise 6 CDRs, three from the VH domain and three from the VL

domain, wherein the humanized antibody, the humanized scFV and fragments thereof bind the same antigen as the parental non-human antibody." Applicants assert that the specification is also enabling for humanized variable domains, humanized antibodies, humanized scFvs and fragments thereof which ***specifically binds*** to a ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. Specifically, Applicants teach at least at paragraphs [064]-[066] and [0136] how to make chimeric antibodies. Applicants teach at least at paragraph [070] and [0137] how to make humanized antibodies. Applicants teach at least at paragraph [040] how to make antigen binding fragments, *e.g.,* Fab, Fab', F(ab')2, Fv, SFv, and scFv. Further, at the time of filing, it was well-known to one skilled in the art how to generate chimeric antibodies, humanized antibodies and antigen binding fragments. For example, several different methodologies were known in the art for making humanized antibodies prior to the filing date of the instant application, see, *e.g.,* Queen *et al.*, *Proc. Natl. Acad. Sci. USA* 86:10029-10033 (1989), US 5,530,101, US 5,585,089, US 5,693,761, US 5,693,762, Selick *et al.*, WO 90/07861, and Winter, US 5,225,539. Moreover, methods of making antigen-binding fragments of antibodies were within the skill of the art, see, *e.g.,* Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269 315 (1994), Ward *et al.* (1989) *Nature* 341:544-546; Bird *et al.* (1988) *Science* 242:423-426; and Huston *et al.* (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883.

Applicants refer the Examiner to MPEP § 2164.01, which states that ***"[a] patent need not teach, and preferably omits, what is well known in the art***. *In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cr. 1991); *Hybritech Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert denied,* 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.,* 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir., 1984)." (Emphasis added). In the present case, there were numerous publications at the time of filing of the present invention disclosing humanized variable domains, humanized antibodies, humanized scFvs and fragments thereof. Applicants submit that the teachings in Applicants' specification, combined with the foregoing well known information, were sufficient to enable one of ordinary skill in the art to generate the claimed antibodies using only routine experimentation. Moreover, with respect to antibodies, the court in Chrion held that because chimeric antibodies were considered nascent technology at the time of filing of the patent at issue, undue experimentation would be required to make and use the claimed chimeric antibodies. *Chiron Corp. v. Genentech, Inc.,* 363 F.3d 1247, 1254 (Fed. Cir.

2004), *cert. denied,* 543 U.S. 1050 (2005). Unlike Chiron, and as noted above, methods of making and using chimeric antibodies, humanized antibodies and antigen-binding fragments were well-known in the art at the time of filing the instant specification. Therefore, the disclosure of the instant specification is commensurate in scope with the claims.

As evidenced by all of the foregoing, the amount of direction and guidance disclosed in the specification, as well as the general knowledge in the art at the time of the invention, is sufficient to enable the skilled artisan to make and use the claimed invention using only routine experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 18 and 25 under 35 U.S.C. §112, first paragraph.

Rejection of Claims 18, 24 and 28 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 18, 24 and 28 under 35 U.S.C. §102(b) as allegedly being anticipated by Hunter *et al.* (U.S. Patent No. 4,954,449) in view of Argaman *et al.* (1974). In particular, the Examiner is of the opinion that

> Hunter et al disclose compositions of human monoclonal antibodies directed to polyribosyl ribitol phosphate...
> The monoclonal antibodies in the composition are directed to pathogenic bacteria that comprise poly ribitol phosphate, and in light of evidence provided by Argaman et shows cross reactivity between H. influenza and Staphylococcus aureus... inherently the compositions of Hunter et al anticipate the instantly claimed invention. (Emphasis added).

Applicants respectfully traverse the foregoing rejection on the grounds that Hunter *et al.* and Argaman *et al.* fail to teach or suggest each and every element of the claimed invention, either expressly or inherently. Reconsideration and withdrawal of the rejection in light of the following discussion is respectfully requested.

For a prior art reference to anticipate a claimed invention, the prior art reference must teach each and every element of the claimed invention. *Lewmar Marine v. Barient* 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Under principles of inherency, "if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates [the claim]." *Mehl/Biophile Int'l Corp. v. Milagraum,*192 F.3d 1362, 1365 (Fed Cir. 1999). To show that the prior art "necessarily" functions in accordance with, or includes the claimed limitations, one must show more than a

mere probability or possibility of the inherent feature's existence. *See SmithKline Beecham Corp. v. Apotex Inc.,* 403 F.3d 1331, 1346 (Fed. Cir. 2005). Therefore, "[i]nherency...***may not be established by probabilities or possibilities***. The mere fact that a certain thing ***may*** result from a given set of circumstances is not sufficient." *Mehl/Biophile,* 192 F.3d 1362 at 1365 (emphasis added) (quoting *Hansgirg v. Kemmer*, 102 F.2d 212, 214 (CCPA 1939)).

The claims, as amended are directed to a pharmaceutical composition comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that ***specifically binds to the ribitol phosphate wall teichoic acid (WTA) of Figure 1A of S. aureus,*** wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks ***nasal colonization*** or infection by *S. aureus* upon administration to a patient.

Hunter *et al.* is directed to monoclonal antibodies directed against the human alpha-polyribosyl ribitol phosphate (PRP) capsular polysaccharide of *H. influenzae* type b, a Gram negative bacteria. At column 5, lines 59-66 of Hunter *et al.,* they disclose that

> [t]he human monoclonal antibody of this invention is a ***very specific reagent*** that can be used to identify PRP antigen in body fluids, and thus diagnose cases of disease caused by a pathogenic microorganism bearing PRP capsular polysaccharide. This antibody has a distinct advantage over currently used polyclonal reagents in its ***lack of cross reactivity with other bacterial and human antigens***. (Emphasis added).

Hunter *et al.* go on to demonstrate that their antibody had ***no effect on the growth of other bacterial strains*** and "point to the specificity of the... antibody for PRP" (see, *e.g.,* column 5, lines 49-58 of Hunter *et al.*). Accordingly, Hunter *et al.* only teach an antibody which ***specifically*** binds to the capsular polysaccharide PRP of the specific Gram negative bacteria, *H. influenzae*. Hunter *et al.* specifically teach that their antibody does <u>not</u> expressly or inherently cross-react and bind other epitopes or bacterial strains. Hunter *et al.* do <u>not</u> teach or suggest an antibody which specifically binds the ribitol phosphate WTA of *S. aureus* (as shown in Figure 1A) and does not significantly cross-react with any other epitopes, as required by the currently pending claims. Furthermore, Hunter *et al.* does not teach or suggest, either expressly or inherently, the claimed antibody, which could be used to alleviate or block ***nasal colonization or infection by S. aureus*** upon administration to a patient.

The secondary reference of Argaman *et al.* fails to make up for the deficiencies of the Hunter reference. Argaman *et al.* is directed to the immunization of rabbits and burros with *H.*

influenzae in order to produce ***antisera which cross reacts with other whole bacteria (i.e., polyclonal antibodies)***, including bacteria of the species *S. aureus*. As discussed above, the pending claims require that the claimed antibody ***specifically*** bind to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. As such, the claimed antibodies are ***specific*** for the ribitol phosphate WTA of *S. aureus* (as shown in Figure 1A) and ***would <u>not</u> significantly cross-react with any other epitopes***. As Argaman *et al.* teach that their antisera cross reacts with several species, Argaman *et al.* fail to teach or suggest the presently claimed antibodies which ***specifically*** bind to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*.

Neither Hunter *et al.* nor Argaman *et al.*, either alone or in combination, expressly or inherently teach or suggest antibodies which ***specifically*** bind to the ribitol phosphate WTA of Figure 1A of *S. aureus*, and therefore neither Hunter *et al.* nor Argaman *et al.*, alone or in combination, anticipate the claimed invention. For the foregoing reasons, rejection of the claimed invention is believed to be improper and Applicants respectfully request that it be reconsidered and withdrawn.

Rejection of Claims 18, 21-25 and 28 Under the Judicially Created Doctrine of Nonstatutory Obviousness-Type Double Patenting

The Examiner has rejected claims 18, 21-25 and 28 under the judicially created doctrine of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 7,169,903 (Attorney Docket No. SYNI-008). In particular, the Examiner is of the opinion that

> [t]he allowed compositions of US Pat. 7,169,903, claims 7-10 include antibodies directed to peptidoglycan and lipoteichoic acid that include monoclonal antibodies directed to N-acetylglucosamine and teichoic acids...
> [t]he instant claims are directed to compositions of monoclonal antibodies directed to teichoic acids plus additional carbohydrates and proteins depending on the species and include monoclonal antibodies directed to GlcNAc (N-acetylglucosamine) modification and cross react with WTA from other staphylococcal species...
> Though the scope of the allowed claims is not identical to the instant claims, the allowed claims are directed to a genus of compositions that comprise antibodies of the instant claims, the instant claims being a species of the invention encompassed by the allowed genus. (Emphasis added).

The instant claims, as amended are directed to a pharmaceutical composition comprising a therapeutically effective amount of a monoclonal antibody or an antigen binding fragment thereof that ***specifically binds to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of S. aureus,*** wherein said therapeutically effective amount of said antibody or fragment thereof alleviates or blocks ***nasal colonization*** or infection by *S. aureus* upon administration to a patient.

Conversely, the claims of the '903 patent are directed to 1) compositions comprising a therapeutically effective amount of a monoclonal antibody, or an antigen-binding portion thereof, that ***specifically binds to peptidoglycan (PepG)*** and 2) compositions comprising such anti-PepG antibodies which specifically bind PepG in combination with an antibody, or antigen-binding fragment thereof, that ***specifically binds to lipoteichoic acid (LTA).***

The pending claims require that the claimed antibody specifically binds to ribitol phosphate wall teichoic acid (WTA) of Figure 1A of *S. aureus*. As discussed in detail above, the claimed antibodies are ***specific for the ribitol phosphate WTA of S. aureus (as shown in Figure 1A)*** and would not significantly cross-react with peptidoglycan or lipoteichoic acid (LTA). In contrast, the issued claims of the '903 patent are directed to compositions comprising antibodies which ***specifically*** bind to peptidoglycan which may further comprise antibodies which ***specifically*** bind to LTA. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' Attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

In addition, Applicants include herewith authorization to charge fees associated with new claims and the extension of time with which to respond, to Deposit Account No. 12-0080, under Order No. SYNI-007RCE2. The Director is also hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. 12-0080, under Order No. SYNI-007RCE2.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: October 3, 2008

Respectfully submitted,

By /Amy E. Mandragouras/
Amy E. Mandragouras, Esq.
Registration No.: 36,207
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicants